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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,868	04/25/2007	Jean-Louis Viovy	121697	5953

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Oliff & Berridge, PLC
P.O. Box 320850
Alexandria, VA 22320-4850

EXAMINER	
WHISENANT, ETHAN C	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,868	VIOVY ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 SEP 08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 30-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

1. The applicant's response (filed 08 SEP 09) to the Office Action has been entered. Following the entry of the claim amendment(s), **Claim(s) 1-28 and 30-39** is/are pending. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 112 - 1ST PARAGRAPH

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

CLAIM REJECTIONS under 35 USC § 112- 1ST PARAGRAPH

3. **Claim(s) 1-28 and 30-39** is/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting a point mutation using heteroduplex analysis, **does not reasonably provide enablement** for the entire scope encompassed by the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make the invention commensurate in scope with these claims without undue experimentation.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d)

the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

In Claim 1, for example, the breadth of the claim encompasses a method in which the concentration of said compound able to undergo a specific base pairing interaction with said mismatch in a liquid medium is 10g/L or greater. The claims thus encompasses a method in which the compound(s) able to undergo a specific base pairing interaction with said mismatch in a liquid medium is/are 10g/L, 25g/L, 50g/L, 75g/L, 100 g/L, etc. A review of the sepecification reveals that experiments at such "high" concentrations are absent. The specification does teach that it is preferable to to have said compounds at 25 g/L, see ¶s [0108] – [0109], however, there is no evidenced presented that assays in which said compounds are present at such concentarations result in a functional method of assaying for the presence or absence of at least one mutation on a strand of nucleic acids paired in duplex form. The "best" experiments disclosed teach compound(s) able to undergo a specific base pairing interaction at concentrations of approximately 7.5 g/L, see for Example 3. Figures 1-6 of the specification show electrophoretic results with "low" concentrations of compound(s) able to undergo a specific base pairing interaction with a mismatch in a liquid medium. **All of the other independent claims (i.e. Claims 3, 5, 25, 27, 31, 32, 34, 38 and 39) in which concentrations of at least 10g/L, or at least 1g/L are recited, likewise fail to comply with the enablement requirement of 35 USC 112, first paragraph).**

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

CLAIM REJECTIONS UNDER 35 USC § 102

5. **Claim(s) 31-32** is/are rejected under 35 U.S.C. 102(a) as being anticipated by Fisher BioReagents exACTGene PCR Kits [copyrighted (2003)].

Fisher BioReagents Advertisement for the exACTGene PCR kit teach a composition (i.e. kit) comprising a compound (i.e. the nucleotide mix comprising 10mM of each nucleotide) which are compounds able to undergo specific base pairing interaction at a concentration of at least 10g/L. At 10 mM of each dNTP the concentration of the dNTPs in the PCR nucleotide mix is approximately 5g /L of each dNTP or a total concentration of all dNTPs of approximately 20g/L (i.e. at least 10g/L). As regards the limitation in Claim 31 that reads "comprising a DNA fragment having a nucleic acid sequence related to a gene on which a point mutation(s) has been associated or putatively associated with a disease or or an increased predisposition to a disease." Note that the exACTGene PCR kit teach a DNA template which is DNA fragment having a nucleic acid sequence related to (i.e. they are both composed of

nucleic acids) a gene on which a point mutation(s) has been associated or putatively associated with a disease or or an increased predisposition to a disease.

35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 102/103

8. **Claim(s) 27-30** is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ruiz-Martinez et al. [Analytical Chemistry 65 : 2851-2858 (1993)].

Claim 27 is drawn to a composition comprising a compound able to undergo specific base pairing interaction at a concentration of at least 1 g/1 being present in a liquid separating medium that comprises at least one polymer at a concentration of at least 1% by weight.

Ruiz-Martinez et al. teach the analysis of DNA sequencing ladders by capillary electrophoresis using linear polyacrylamide separating medium. The LPA comprises at least one polymer at a concentration of at least 1% by weight. Note that at the point of the assay taught by Ruiz-Martinez et al. where the DNA sequencing ladders are loaded onto the capllaries the claimed composition is obtained. The DNA sequencing ladders loaded will comprise a compound (i.e. the unincorporated dNTPs) able to undergo a specific base pairing interaction at a concentration of at least 1g/L. Note that the claim language does not require that the compound(s) be present at the concentration recited only that they have the capability to undergo a specific base pairing interaction at a concentration of at least 1g/L. The unincorporated dNTPs have the ability (i.e. they are able to/they are capable of) undergo a specific base pairing interaction at a concentration of at least 1g/L.

Claim 28 is drawn to an embodiment of the composition of Claim 27, wherein the compounds able to undergo a specific base pairing interaction includes at least two groups suitable for hydrogen bonding, in an orientation, polarity and spacing compatible with the creation of attractive interaction with at least one of the bases A, T, G, C, and U.

Ruiz-Martinez et al. teach this limitation in that the compounds (i.e. the unincorporated dNTPs) able to undergo a specific base pairing interaction includes at least two groups suitable for hydrogen bonding, in an orientation, polarity and spacing compatible with the creation of attractive interaction with at least one of the bases A, T, G, C, and U.

Claim 30 is drawn to an embodiment of the composition of Claim 27, wherein said a liquid separating medium comprises one member selected from a defined group which includes a sieving polymer.

Ruiz-Martinez et al. teach this limitation in that the linear polyacrylamide separating medium of the capillaries is a sieving polymer.

9. Claim(s) 31-32 is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Perkin Elmer Cetus [GeneAmp™ DNA amplification kit (1988)].

Claim 31 is drawn to composition comprising a DNA fragment having a nucleic sequence (i.e. a nucleic acid sequence?) related to a gene on which a point mutation(s) have been associated or putatively associated with a disease or an increase predisposition to a disease, and at least one compound able to undergo specific base pairing interaction at a concentration of at least 10g/L, wherein said compound able to undergo specific base pairing interaction includes at least two groups suitable for hydrogen bonding, in an orientation, polarity and spacing compatible with a creation of attractive interaction with at least one of bases A,T, G, C, and U.

Perkin Elmer Cetus teach a composition (i.e. a kit) comprising a DNA fragment and compound able to undergo specific base pairing interactions at a concentration of 10g/L (i.e. any of the dNTPs will have this capability). As regards the limitation that the DNA fragment have "a nucleic acid sequence related to a gene on which a point mutation(s) have been associated or putatively associated with a disease or an increase predisposition to a disease. This limitation is directed towards the intended use of the composition and, therefore, fails to further limit the claimed invention. As regards the limitation which requires that compound able to undergo specific base pairing interactions at a concentration of at least 10g/L, it is admitted that Perkin Elmer Cetus is silent in this regard, however, this limitation is directed towards the intended use of the composition and as such fails to further limit the composition. Furthermore any of the dNTPs of the Perkin-Elmer kit meet this limitation in that the dNTPs are compounds able to undergo specific base pairing interactions at a concentration of at least 10g/L.

Claim 32 is drawn to composition comprising a compound able to undergo specific base pairing interaction at a concentration of a least 10g/L and a pair of DNA probes, wherein said compound able to undergo specific base pairing interaction includes at least two groups suitable for hydrogen bonding, in an orientation, polarity and spacing compatible with the-acreation of attractive interaction with at least one of the-bases A, T, G, C, and U.

Perkin Elmer Cetus teach a composition (i.e. a kit) comprising a compound (i.e. the nucleotides) capable of undergoing specific base pairing interaction at a concentration of a least 10g/L and a pair of DNA probes. Also, note that the nucleotides of the PE kit are able to undergo specific base pairing interaction and include at least two groups suitable for hydrogen bonding, in an orientation, polarity and spacing compatible with the creation of attractive interaction with at least one of the bases A, T, G, C, and U.

10. Claim(s) 33 is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ruiz-Martinez et al. [Analytical Chemistry 65 : 2851-2858 (1993)] in view of the Stratagene Catalog [p.39 (1988)].

Claim 33 is drawn to a kit comprising a composition of Claim 27.

Ruiz-Martinez et al. teach a method of preparing DNA sequencing ladders with the subsequent analysis of said ladders by capillary electrophoresis using linear polyacrylamide separating medium. The LPA comprises at least one polymer at a concentration of at least 1% by weight. Ruiz-Martinez et al. does not teach a kit however, as evidenced by the Stratagene Catalog it was routine in the art to gather all of the reagents needed to practice a method and to then assemble said reagents into a kit.. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to package the reagents

needed to practice the method reasonably suggested by Salazar et al in view of Eggerding, Hossian et al. or Qiagen News and Ciulla et al. into a kit format. The ordinary artisan would have been motivated to make the modification recited above for the expected benefits of convenience and cost-effectiveness taught by the Stratagene Catalog.

11. Claim(s) 34-35 is/are rejected under 35 U.S.C. 103(a) as obvious over Saiki et al. [Nature 324 : 163-166 (1986)].

Saiki et al. teach a method of assaying for a mutation in a nucleic acid which comprises all of the limitations of Claim 34. Note that in Saiki et al. the dNTPs are present at a concentration of 1.5mM each. Thus Saiki et al teach performing their PCR reactions in the presence of at least two primers and a pool of compounds able to undergo specific base pairing interaction with nucleotides . Admittedly, Saiki et al. do not teach performing their PCR reaction using the dNTPs at the concentration recited (i.e. at least 10g/L). At 1.5mM of each dNTP the concentration of the dNTPs in the Saiki et al reaction mixture(s) is approximately 3.347g /L (i.e. at least 1g/L). However, where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

12. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

13. Claim(s) 1-28 and 30-39 is/are rejected and/or objected to for the reason(s) set forth above.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30 am -5:30 pm EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634